Impact de la vaccination en France

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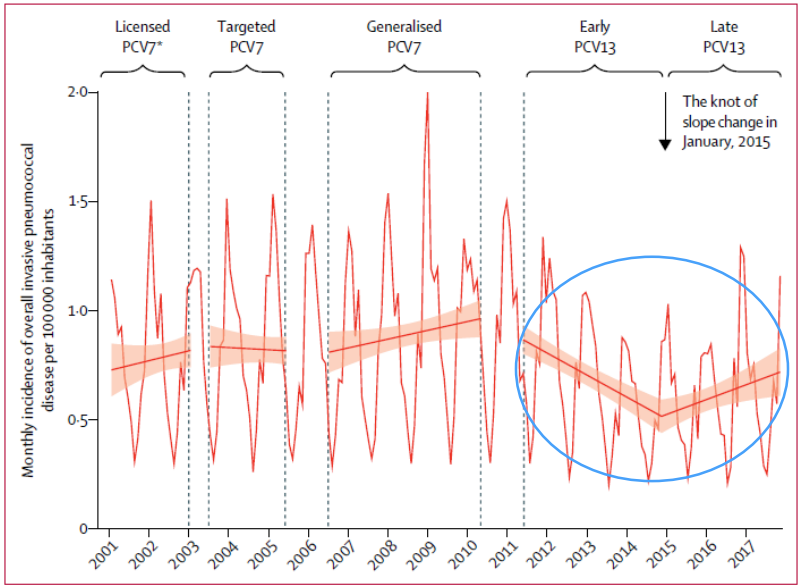
Déclaration d'intérêts 2018 - 2020

- Liens durables ou permanents : Néant
- Intérêts financiers : Néant
- Interventions ponctuelles : Pfizer, Bruker
- Intérêts indirects : Pfizer, MSD-Vaccins, bioMérieux

Invasive pneumococcal disease incidence in children and adults in France during the pneumococcal conjugate vaccine era: an interrupted time-series analysis of data from a 17-year national prospective surveillance study

Naïm Ouldali, Emmanuelle Varon, Corinne Levy, François Angoulvant, Scarlett Georges, Marie-Cécile Ploy, Marie Kempf, Julie Cremniter, Robert Cohen, Daniel Levy Bruhl*, Kostas Danis*



EPIBAC Network, ORP & CNRP

75903 patients (<16 years 12%)

- 7258 meningitis
- 68645 non-meningitis IPD

2010-2014: - 43.6% (95% CI -39.4 to -47.9),

2015-2017: + 1.8% per month, (95% CI 1.0 to 2.6)

IPD cases averted:

- 7 600 meningitis (95% CI 6 775 to 8 425)
- 37 031 non-meningitis (95% CI 30 118 to 43 944)

Lancet Infect Dis. 2020 Jul 20:S1473-3099(20)30165-1

French *Streptococcus pneumoniae* network

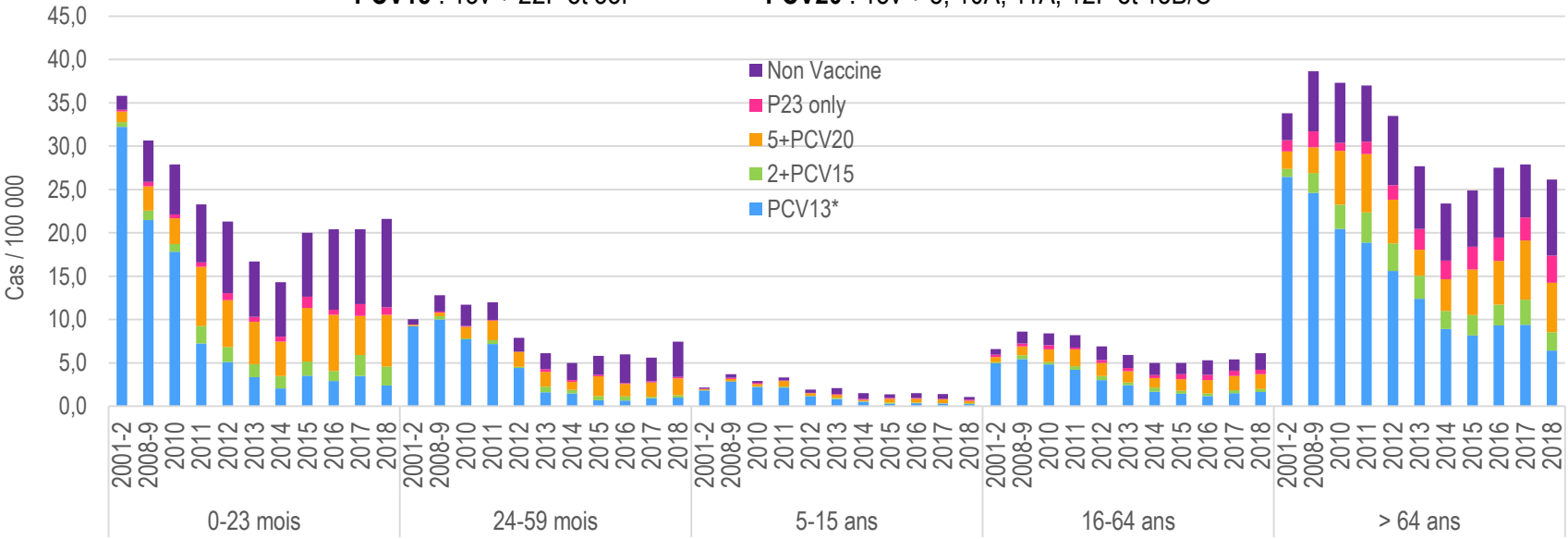
- **Pneumococcal invasive isolates from the French national network ORP, 2001 to 2018**
  - All CSF isolates are sent to NRCP
  - Blood isolates
    - All children (< 15 years) isolates are sent to NRCP
    - Adults 25% of ORP isolates are sent to NRCP
  - Serotyped IPD strains in France
    - < 16 years: 80%
    - Adults: 25%

Age groups	Meningitis	Bacteremia	Total IPD
0-23 months	1 252	1 917	3 169
24-59 months	311	1 328	1 639
5-15 years	412	1 038	1 450
16-64 years	2 890	4 102	6 992
> 64 years	1 671	5 361	7 032
All ages	6 536	13 746	20 282

Incidence rate of IPD according to group of serotypes, France

PCV13 : 4, 6B, 9V, 14, 18C, 19F, 23F + 1, 3, 5, 6A, 7F, 19A

PCV15 : 13v + 22F et 33F **PCV20** : 15v + 8, 10A, 11A, 12F et 15B/C



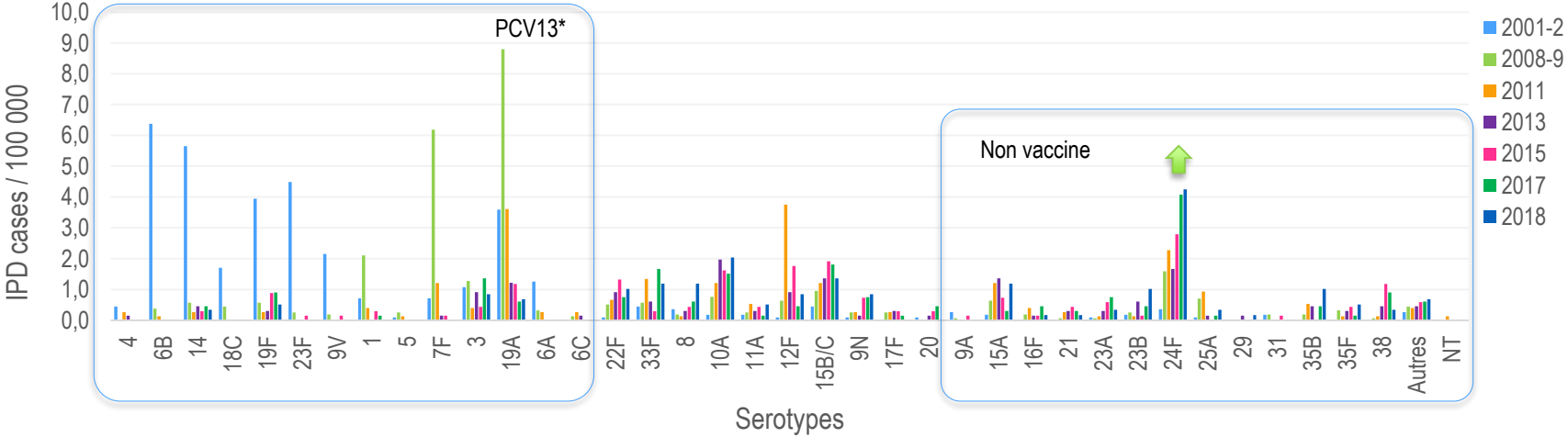
Significant decrease in all age groups

→ Partial replacement

Incidence rate: EPIBAC-SantéPublique France
CNRP-ORP, unpublished data

Serotype specific incidence rate of IPD, children < 2 years

Direct effect : quasi-eradication of PCV13 IPD (except 19F, 19A and 3)
Emerging non vaccine types: **24F** >> 15B/C, 10A, 22F or 33F

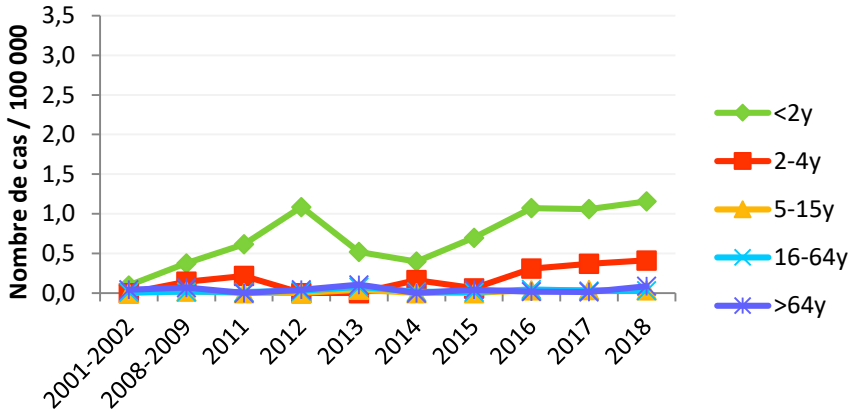


IPD < 2 years	2001-02	2008-09	2011	2013	2015	2017	2018
Number of cases	399	481	174	110	136	135	127

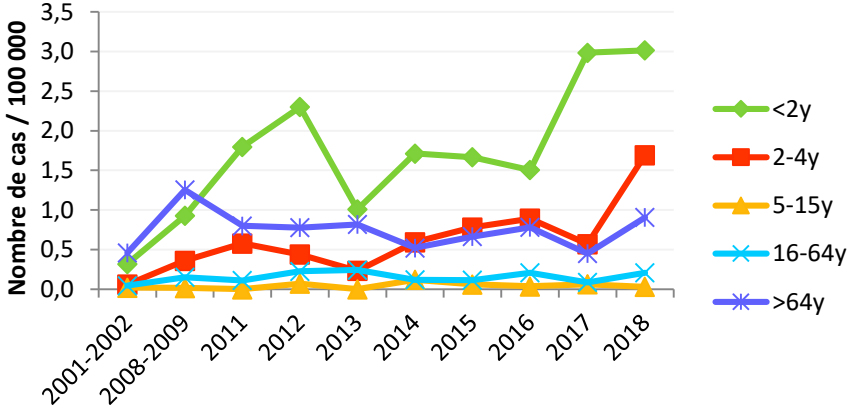
Incidence rate: EPIBAC-SantéPublique France
CNRP-ORP, unpublished data

Trends in incidence rate of serotype 24F IPD according to age group

Meningitis



Bacteremia

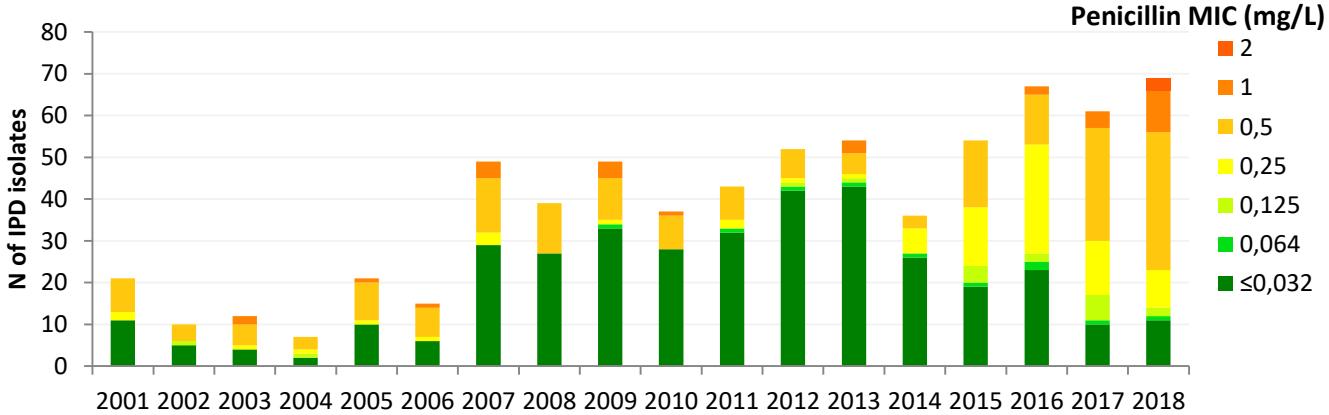


Leading cause of IPD among children < 2 years
Unfrequent in adults (> 15 years)

Incidence rate: EPIBAC-Santé Publique France
CNRP-ORP, unpublished data

Penicillin susceptibility of serotype 24F IPD isolates

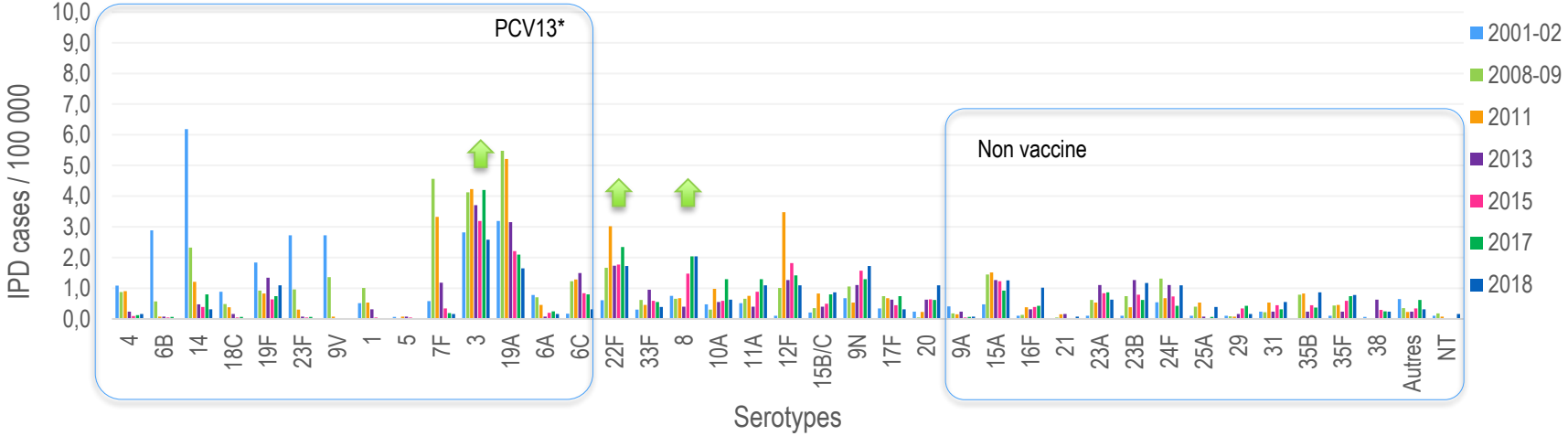
Leading cause of IPD among children < 2 years
Increasing number of penicillin non-susceptible serotype 24F isolates



CNRP-ORP, 2019 - unpublished data

Serotype specific incidence rate of IPD, adults > 64 years

Indirect effect : dramatic decrease in PCV13 IPD except for serotype 3, 19A and 19F
Emerging non PCV13 serotypes: 22F, 8

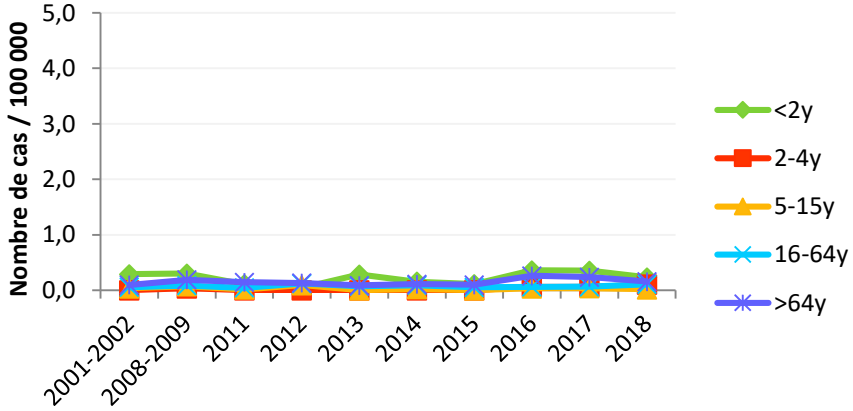


IPD > 64 years	2001-02	2008-09	2011	2013	2015	2017	2018
Number of cases	994	881	490	351	507	452	334

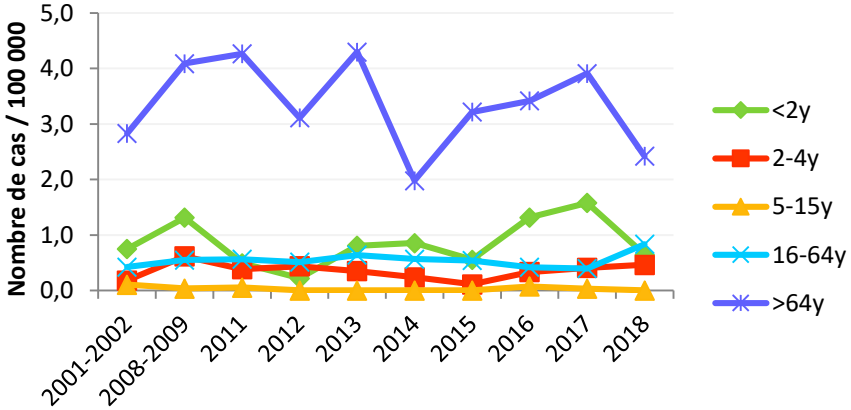
Incidence rate: EPIBAC-SantéPublique France
CNRP-ORP, unpublished data

Trends in incidence rate of serotype 3 IPD according to age group, France

Meningitis



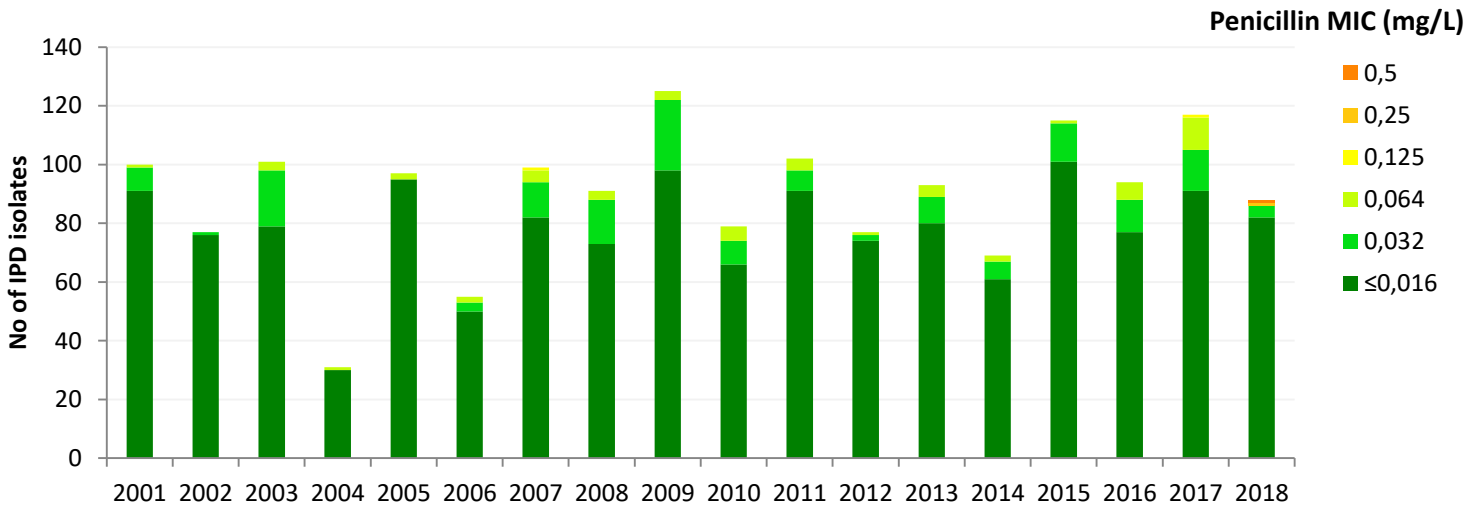
Bacteremia



Leading cause of PCV13 IPD in adults > 64 years
Ranking 5th in children < 2 years

Incidence rate: EPIBAC-Santé Publique France
CNRP-ORP, unpublished data

Penicillin susceptibility of serotype 3 IPD isolates

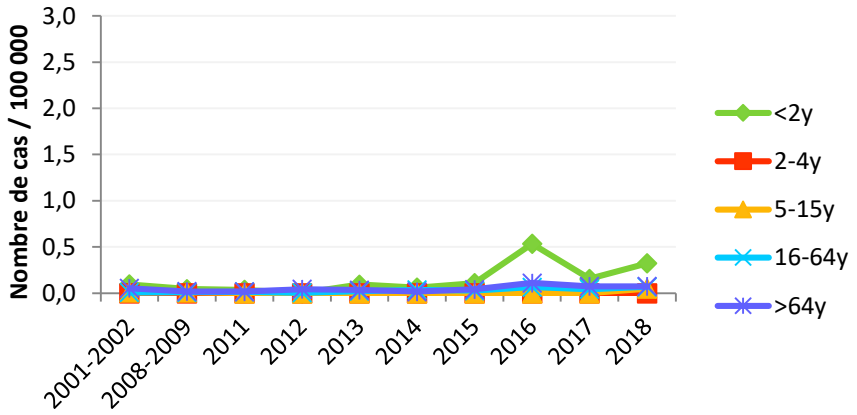


Leading cause of PCV13 IPD in adults > 64 years
Ranking 5th in children < 2 years
Beta-lactam susceptible

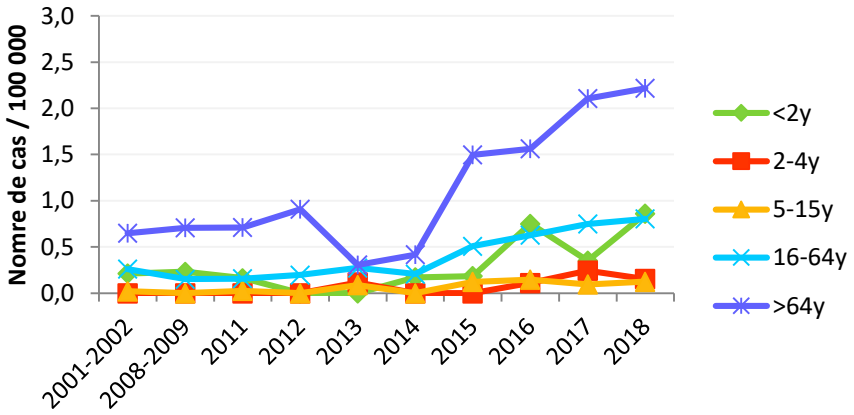
CNRP-ORP, 2018 - unpublished data

Trends in incidence rate of serotype 8 IPD according to age group

Meningitis



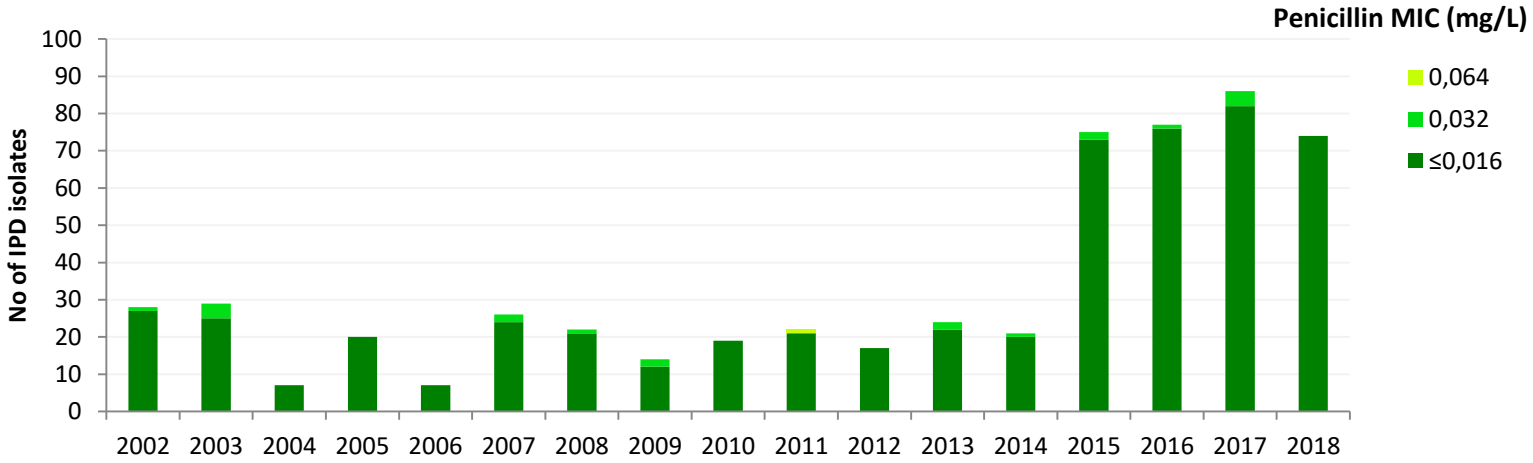
Bacteremia



Leading cause of non PCV13 type among IPD in adults > 64 years
2nd emerging non PCV13 among IPD in children < 2 years

Incidence rate: EPIBAC-Santé Publique France
CNRP-ORP, unpublished data

Penicillin susceptibility of serotype 8 IPD isolates

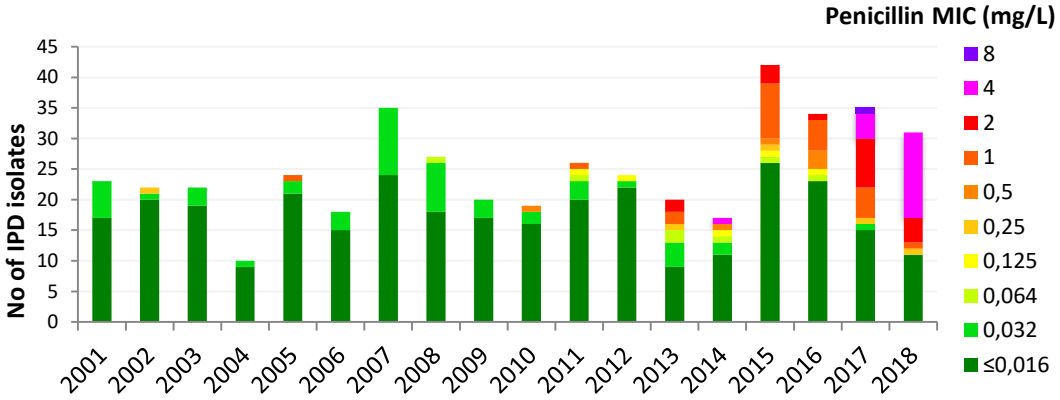


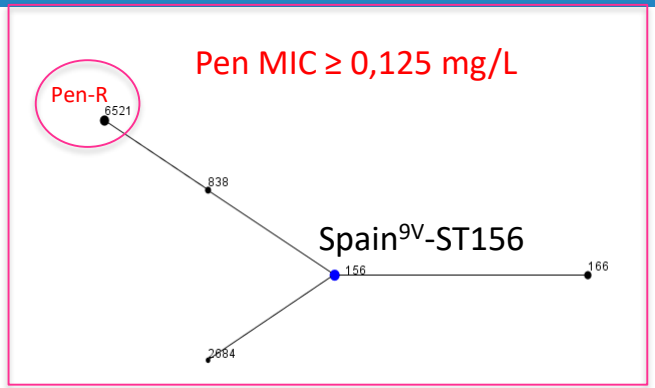
Leading cause of non PCV13 type among IPD in adults > 64 years
2nd emerging non PCV13 among IPD in children < 2 years
Increase of penicillin-susceptible isolates

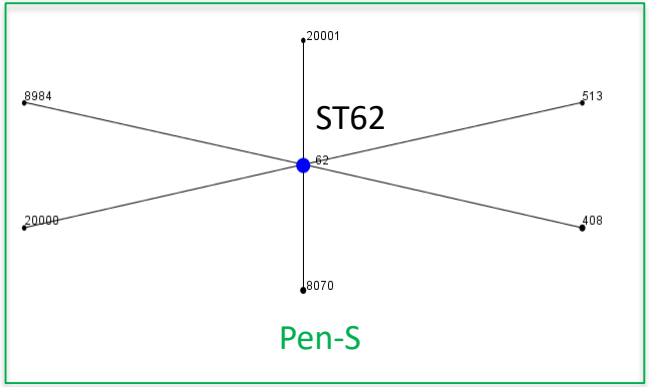
CNRP-ORP, unpublished data

Penicillin susceptibility of serotype 11A IPD isolates

Non PCV13 emerging serotype among IPD in adults > 64 years
Good colonizer, low disease potential in children < 2 years
Emerging beta-lactam non susceptible isolates







- Penicillin-resistant serotype 11A isolates reported in south-western Europe

Two multi-fragment recombination events resulted in the β-lactam-resistant serotype 11A-ST6521 related to Spain9V-ST156 pneumococcal clone spreading in south-western Europe, 2008 to 2016

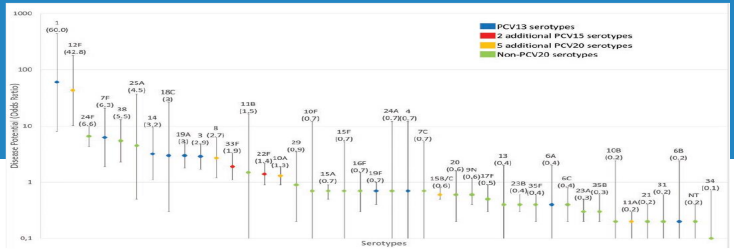
Gonzalez-Diaz et al. Euro Surveill. 2020; 25(16): 1900457

IPD serotypes (%) covered by vaccines, France 2018

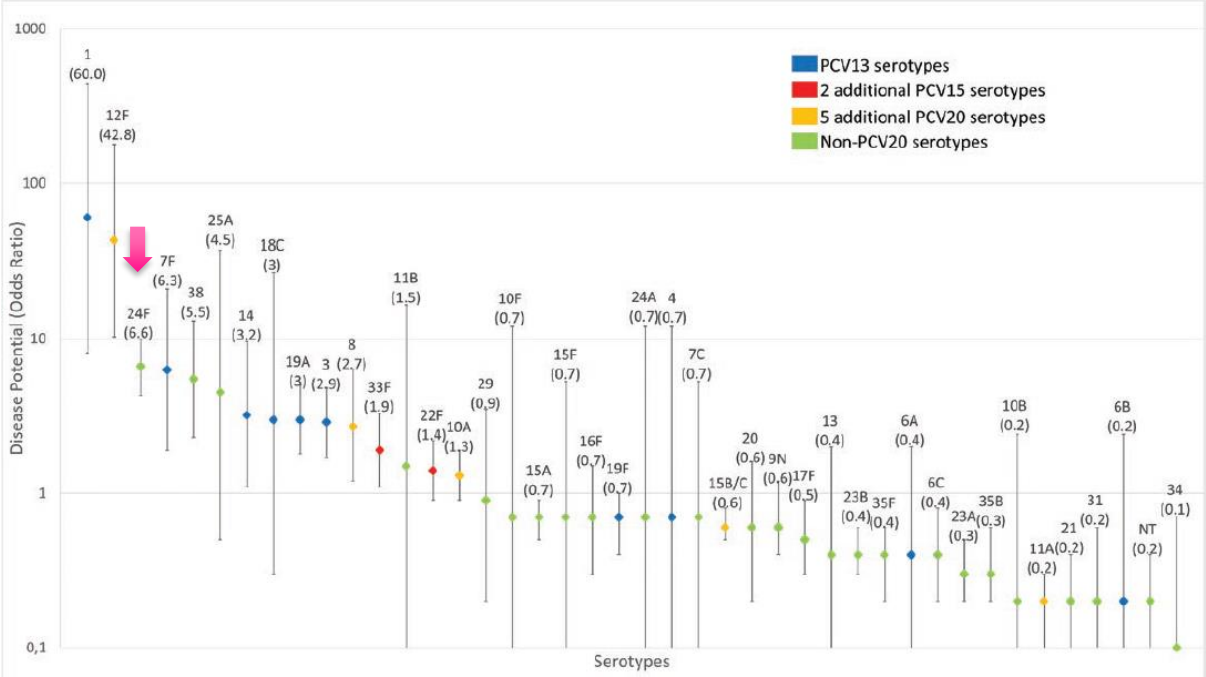
	PCV13	2+PCV15	5+PCV20	PPV23 only	Non vaccine	Total
<15 years	14%	9%	27%	5%	46%	100%
15-64 years	25%	5%	28%	8%	33%	100%
> 64 years	23%	8%	22%	12%	35%	100%
Total	22%	7%	27%	7%	37%	100%

	PCV13	PCV15	PCV20	PPV23
<15 years	14%	22%	49%	54%
15-64 years	25%	31%	59%	67%
> 64 years	23%	31%	53%	65%

CNRP-ORP, unpublished data

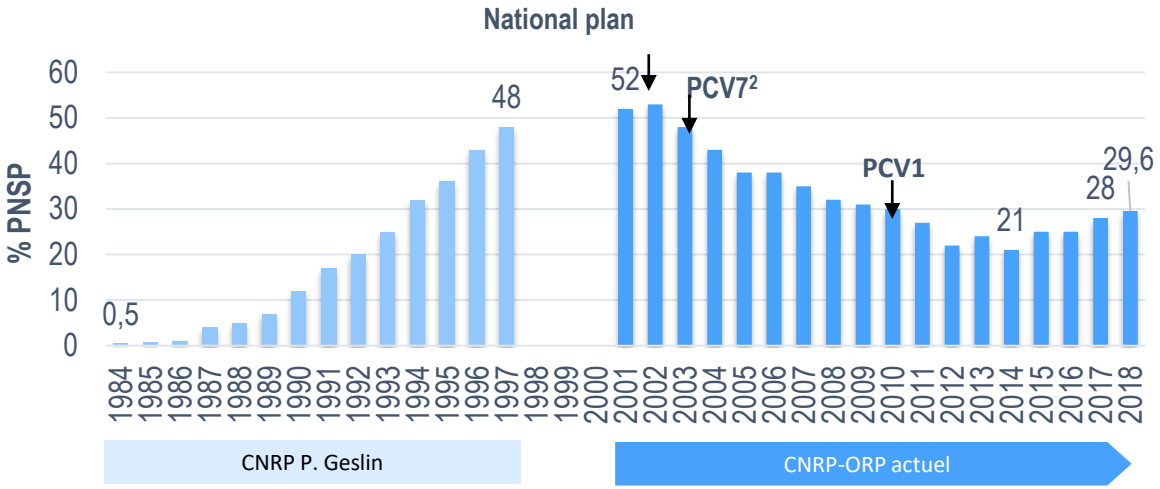


Serotypes isolated from children aged 6 months to 10 years, from 2012 to 2018 (1 385 IPD vs 1 034 healthy carriers)



Clin Infect Dis. 2020 Jul 4:ciaa917.

Penicillin non-susceptible pneumococci (PNSP, %)



1984-2017: 64130 isolates

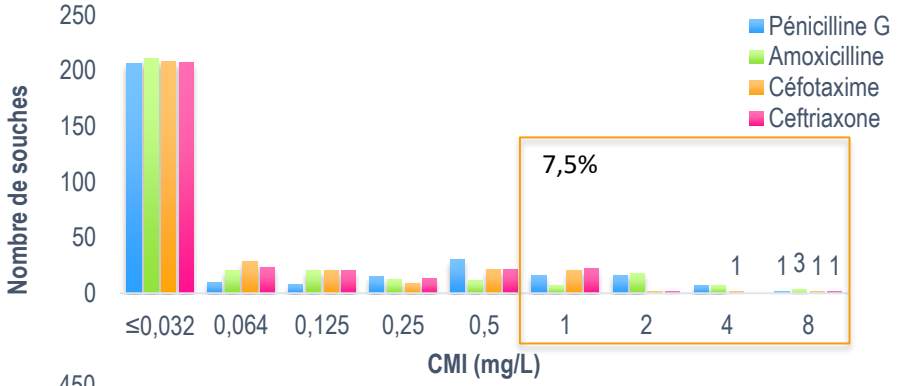
[1]http://www.sante.gouv.fr/htm/actu/34_01.htm

[2]Pneumococcal conjugate vaccine (PCV)

CNRP-ORP, unpublished data

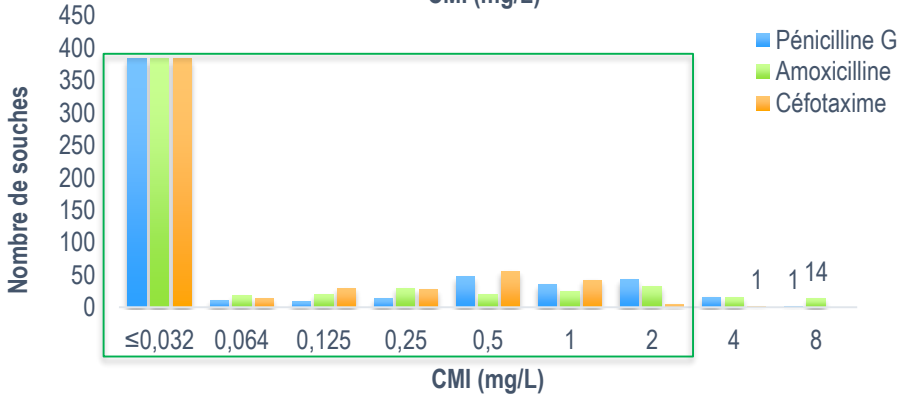
IPD isolates: β-lactam susceptibility in 2018

Méningites



7.5% of meningitis isolates were not susceptible to cefotaxime (MIC > 0.5 mg/L) (CA-SFM EUCAST)

Bactériémies

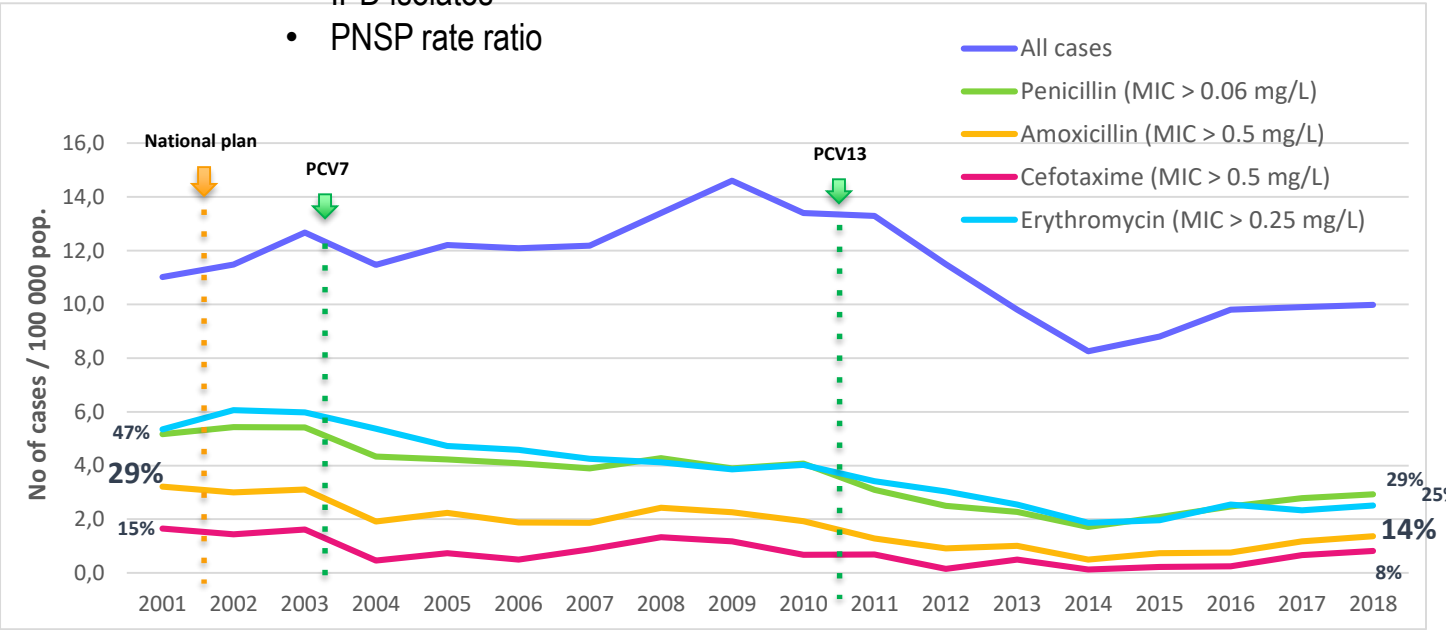


95% of bacteremia isolates are susceptible to amoxicillin (MIC < 2 mg/L) when considering pneumonia (CA-SFM EUCAST)

CNRP-ORP, unpublished data

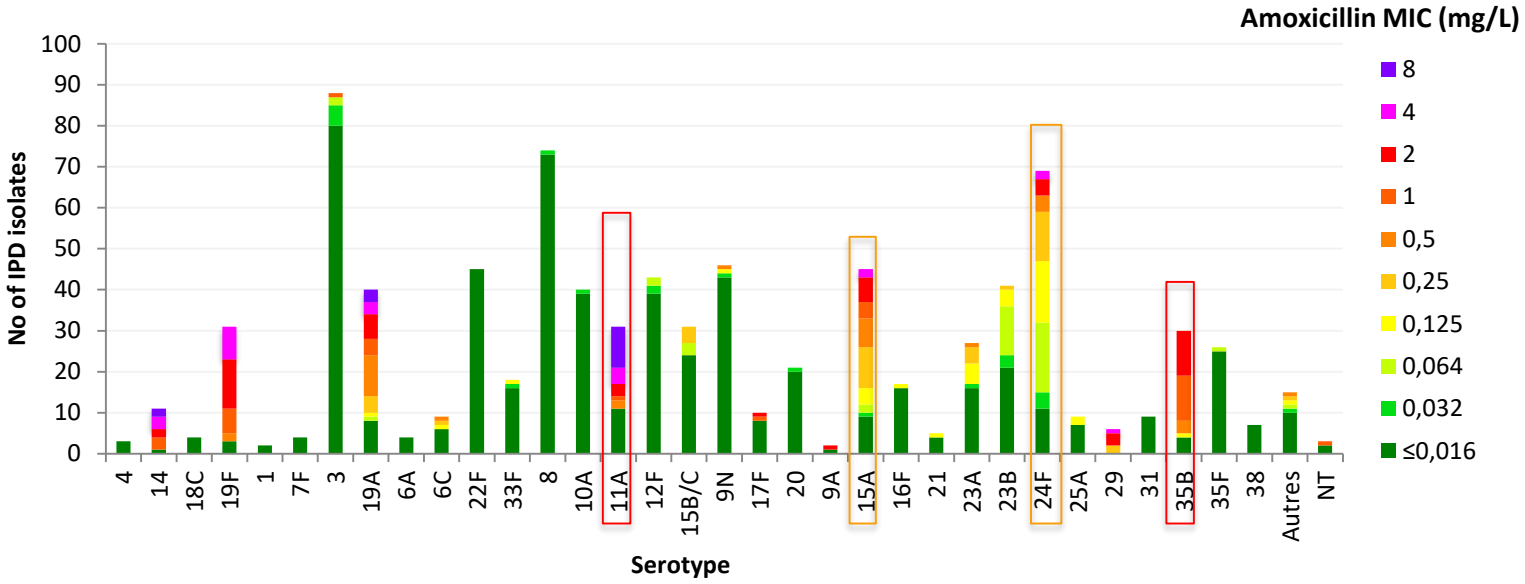
Antibiotic susceptibility among IPD isolates, France, 2001-2017

Decrease in
- IPD isolates
- PNSP rate ratio



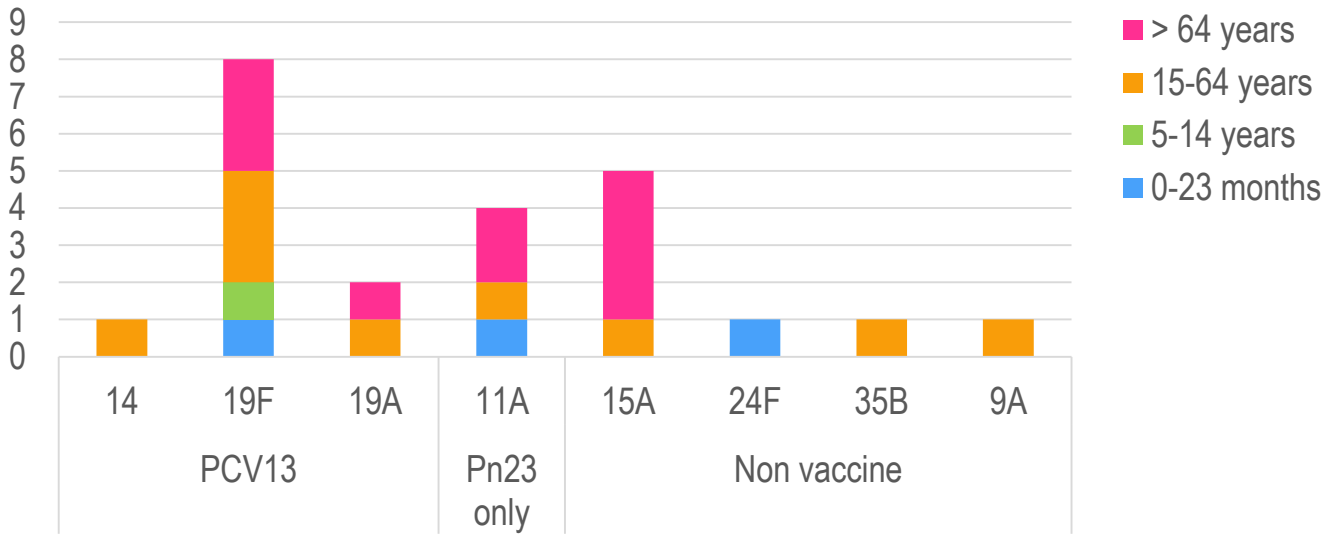
Incidence rate: EPIBAC-Santé Publique France
CNRP-ORP, unpublished data

Amoxicillin susceptibility of IPD isolates according to serotype



CNRP-ORP, unpublished data

Meningitis isolates CTX non-susceptible, by serotype and age group



Summary

- **Since the PCVs introduction the distribution of serotypes has dramatically changed**
  - In the population targeted by the vaccine: children < 2 years
  - In other age groups
    - ↘ ↘ ↘ **PCV serotypes except 3 +++ 19F and 19A**
    - ↗ ↗ **various non-vaccine serotypes**
      - Penicillin-susceptible: **8, 22F** and 9N, 10A
      - PNSP : **24F** >> 11A
- **Leading to change in antibiotic susceptibility and in pattern of pneumococcal disease**
- **The high level of plasticity of the pneumococcal genome can promote lineages escaping PCVs, *ie* with non vaccine type, but with the genetic background of earlier vaccine type predominant clones**
- **Results from our 17-year surveillance study and current epidemiological data highlight the value of vaccination in children and in adults at-risk populations**
- **This is of particular importance at the COVID era**

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http://cnr-pneumo.fr